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Date of Deposit: April 2, 2003

Attorney Docket No. VP1645-101 US

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645

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Chao Lin and Anne Dak-Yee Kwong  
ASSIGNEE: Vertex Pharmaceuticals Incorporated  
SERIAL NUMBER: 10/060,738 CONFIRMATION NO.: 7008  
FILING DATE: January 30, 2002 GROUP ART UNIT: 1645  
FOR: A QUANTITATIVE ASSAY FOR NUCLEIC ACIDS

April 2, 2003  
Cambridge, Massachusetts 02139

Commissioner for Patents  
Washington, D.C. 20231

**INFORMATION DISCLOSURE STATEMENT**

Pursuant to the duty of disclosure under 37 C.F.R. §§ 1.56, 1.97 and 1.98, Applicants hereby make of record the documents listed below and on the attached modified Form PTO-1449 (submitted in duplicate) in the above-identified application, copies of which are submitted herewith. The order of presentation of the references should not be construed as an indication of the importance of the references.

This Information Disclosure Statement is being filed:

- within three months of the filing date of the National Application;
- within three months of the filing date of the entry of the National Stage, as set forth in 37 C.F.R. § 1.491, in an International Application; or
- before the mailing date of a first Office Action on the merits in the above-identified case.

Accordingly, no fee or certification is required. 37 C.F.R. § 1.97.

The documents were cited in a February 27, 2003 International Search Report (copy enclosed) in this application's counterpart PCT Application (PCT/US02/02653).

Applicants request that these documents: (1) be fully considered by the Examiner during examination of this application, and (2) be printed on any patent that may issue from this

APPLICANTS: **Lin, et al.**  
U.S.S.N.: **10/060,738**

application. Applicants also request that a copy of the enclosed form PTO-1449 duly initialed by the Examiner be forwarded to the undersigned with the next communication.

By submitting this Information Disclosure Statement, the Applicant makes no representation that: (1) a search has been performed, of the extent of any search performed, or that more relevant information does not exist; (2) the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b); and (3) the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. § 102.

Please charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0725, Reference No. VPI/01-101 US.

Respectfully submitted,

  
Lisa A. Dixon/Reg. No. 40,995  
Attorney(s) for Applicants  
c/o Vertex Pharmaceuticals Incorporated  
130 Waverly Street  
Cambridge, Massachusetts 02139  
Tel: (617) 444- 6396  
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Modified Form 1449/PTO		Application Number	10/060,738
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		Filing Date	January 30, 2002
(use as many sheets as necessary)		First Named Inventor	Chao Lin
		Group Art Unit	1645
		Examiner Name	Not Yet Assigned
		Attorney Docket Number	VPI/01-101 US

U.S. PATENT DOCUMENTS						
Exam Initials	Cite No.	U.S. Patent Document No.	Issue Date	Name of Patentee(s) or Applicant(s)	Class	Sub Class
	A1	5,952,202	14-Sep-1999	The Perkin Elmer Corporation		Filing Date If Appropriate 26-Mar-1998

FOREIGN PATENT DOCUMENTS					
Exam Initials	Cite No.	Foreign Patent Document Office Number	Name of Patentee(s) or Applicant(s)	Date of Publication	Translation Yes No
	B1	WO 02/061149	Vertex Pharmaceuticals Incorporated	08-August-2002	
	B2	WO 00/29613	Fondazione Centro San Raffaele Del Monte Tabor	25-May-2000	

OTHER NON PATENT LITERATURE DOCUMENTS		
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	C1	Blight, K.J., et al., "Efficient Initiation of HCV RNA Replication in Cell Culture," <i>Science</i> , 290:1972-1974 (2000).
	C2	Kleiber, J., et al., "Performance Characteristics of a Quantitative, Homogeneous TaqMan RT-PCR Test for HCV RNA," <i>J. Mol. Diag.</i> , 2(3):158-166 (2000).

\* a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, U.S.S.N. \_\_\_\_\_, filed \_\_\_\_\_, and relied upon for an earlier filing date under 35 U.S.C. §120 (continuation, continuation-in-part, and divisional applications).

Examiner Signature		Date Considered	
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered.

Include copy of this form with next communication to applicant.



ocket No.: VPI/01-101 US

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**Certificate Of Mailing Under 37 C.F.R. § 1.10**

Express Mailing No. EU 821 024 295 US

Date of Deposit: April 2, 2003

I hereby certify that the following documents:

1. Information Disclosure Statement (in duplicate);
2. Copy of International Search Report;
3. PTO-1449 Form (duplicate);
4. Cited references A1, and B1-B2, C1-C2; and
5. this return postcard receipt.

are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. §1.10 on the date indicated above and is addressed to the Commissioner for Patents, Washington D.C. 20231

Karen DiRocco  
(type or printed name of person mailing document(s))

*Karen DiRocco*  
(signature of person mailing document(s))

PATENT COOPERATION TREATY

"DOCKETED FOR: 4/29/03"

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
 VERTEX PHARMACEUTICALS INC.  
 Attn. GOVINDASWAMY, Nandakumar  
 130 Waverly Street  
 Cambridge, MA 02139-4242  
 UNITED STATES OF AMERICA

PCT

NOTIFICATION OF TRANSMITTAL OF  
 THE INTERNATIONAL SEARCH REPORT  
 OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing  
 (day/month/year)

27/02/2003

Applicant's or agent's file reference  VP101-101	<b>FOR FURTHER ACTION</b>	See paragraphs 1 and 4 below
International application No.  PCT/US 02/ 02653	International filing date (day/month/year)	30/01/2002
Applicant  <b>VERTEX PHARMACEUTICALS INCORPORATED</b>		

1.  The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3.  **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau.

If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for International publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority  
 European Patent Office, P.B. 5818 Patentlaan 2  
 NL-2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Wolfgang Hingel

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the International application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the International application is English, the letter must be in English; if the language of the International application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

**The following examples illustrate the manner in which amendments must be explained in the accompanying letter:**

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### **"Statement under article 19(1)" (Rule 46.4)**

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### **Consequence if a demand for international preliminary examination has already been filed**

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### **Consequence with regard to translation of the international application for entry into the national phase**

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

**PATENT COOPERATION TREATY**  
**PCT**

**INTERNATIONAL SEARCH REPORT**

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>VP 101-101</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 02/ 02653</b>	International filing date (day/month/year) <b>30/01/2002</b>	(Earliest) Priority Date (day/month/year) <b>30/01/2001</b>
Applicant <b>VERTEX PHARMACEUTICALS INCORPORATED</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
  - contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  **Certain claims were found unsearchable** (See Box I).

3.  **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

**None of the figures.**

**INTERNATIONAL SEARCH REPORT**

National Application No  
PCT/US 02/02653

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C12Q1/70 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

MEDLINE, EPO-Internal, BIOSIS, EMBASE, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 29613 A (SALVATORI FRANCESCA ; SCARLATTI GABRIELLA (IT); LUSSO PAOLO (IT); M) 25 May 2000 (2000-05-25) page 4, line 9 -page 10, line 4 claims 1,5,9	1-9
Y	---	10-16
Y	BLIGHT K J ET AL: "EFFICIENT INITIATION OF HCV RNA REPLICATION IN CELL CULTURE" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, US, vol. 290, 8 December 2000 (2000-12-08), pages 1972-1974, XP002951271 ISSN: 0036-8075 page 1973, right-hand column figure 3 ---	10-16
	---	-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

4 February 2003

27/02/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Ulbrecht, M

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 02/02653

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>KLEIBER J ET AL: "Performance characteristics of a quantitative, homogeneous TaqMan RT-PCR test for HCV RNA." THE JOURNAL OF MOLECULAR DIAGNOSTICS: JMD. UNITED STATES AUG 2000, vol. 2, no. 3, August 2000 (2000-08), pages 158-166, XP002229738 ISSN: 1525-1578 page 159, left-hand column, paragraph 2 page 160</p> <p>---</p>	16
A	<p>US 5 952 202 A (AOYAGI KAZUKO ET AL) 14 September 1999 (1999-09-14) column 7, line 17 - line 55 claims 1,7</p> <p>-----</p>	1-9

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No  
PCT/US 02/02653

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
WO 0029613	A 25-05-2000	IT AU WO EP JP	MI982491 A1 1272000 A 0029613 A1 1131466 A1 2002530090 T	17-05-2000 05-06-2000 25-05-2000 12-09-2001 17-09-2002
US 5952202	A 14-09-1999	AU EP WO	3372799 A 1104487 A1 0116367 A1	26-03-2001 06-06-2001 08-03-2001